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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/599,729	10/06/2006	Jong Soo Woo	Q97584	3327
23373	7590	03/30/2010	EXAMINER	
SUGHRUE MION, PLLC 2100 PENNSYLVANIA AVENUE, N.W. SUITE 800 WASHINGTON, DC 20037			FISHER, ABIGAIL L	
			ART UNIT	PAPER NUMBER
			1616	
			NOTIFICATION DATE	DELIVERY MODE
			03/30/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No. 10/599,729	Applicant(s) WOO ET AL.	
	Examiner ABIGAIL FISHER	Art Unit 1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-17 is/are pending in the application.
- 4a) Of the above claim(s) 16 and 17 is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-15 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 06 October 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>10/6/06; 12/6/06</u> . | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

Claims 1-17 are pending

Restrictions

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-15, drawn to a sustained release formulation.

Group II, claim(s) 16-17, drawn to a method of preparing a sustained release formulation.

An international application should relate to only one invention or, if there is more than one invention, the inclusion of those inventions in one international application is only permitted if all inventions are so linked as to form a single general inventive concept (PCT Rule 13.1). With respect to a group of inventions claimed in an international application, unity of invention exists only when there is a technical relationship among the claimed inventions involving one or more of the same or corresponding special technical features.

The expression "special technical features" is defined in PCT Rule 13.2 as meaning those technical features that define a contribution which each of the inventions, considered as a whole, makes over the prior art. The determination is made

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on the contents of the claims as interpreted in light of the description and drawings (if any). Whether or not any particular technical feature makes a "contribution" over the prior art and therefore constitutes a "special technical feature," should be considered with respect to novelty and inventive step.

The inventions listed as Groups I-II do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: The common technical feature in all groups is composition comprising HMG-CoA reductase inhibitor, solubilizing agent, stabilizing agent, carrier and gel hydration accelerator. This element cannot be a special technical feature under PCT Rule 13.2 because the element is shown in the prior art. Gutierrez-Rocca et al. (US Patent No. 6524615) discloses a composition comprising the claimed ingredients. Gutierrez-Rocca et al. claim a sustained or prolonged release pharmaceutical unit dosage form comprising a hard shell capsule and a formulation comprising (1) water insoluble medicament such as atorvastatin, simvastatin, lovastatin (all HMG-CoA reductase inhibitors); (2) a high melting fatty acid ester; (3) low viscosity oil (wherein 2 and 3 read on carrier); (4) a cellulosic polymer such as methocel E series and K series which read on gel hydration accelerator; (4) a non-ionic surfactant such as poloxamers and d-2-tocophenyl polyethylene glycol 1000 succinate (which read on solubilizer) (claim 1). While Gutierrez-Rocca et al. do not claim a stabilizer it is taught that pharmaceutically acceptable excipients can be added such as stabilizers/antioxidants like butylated hydroxyl toluene or ascorbic acid (column 6, lines 6-8). Therefore, it would have been

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obvious to one of ordinary skill in the art to add butylated hydroxyl toluene or ascorbic acid in order to stabilize the composition as taught by Gutierrez-Rocca et al.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a invention to be examined even though the requirement may be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse. Traversal must be presented at the time of election in order to be considered timely. Failure to timely traverse the requirement will result in the loss of right to petition under 37 CFR 1.144. If claims are added after the election, applicant must indicate which of these claims are readable on the elected invention.

If claims are added after the election, applicant must indicate which of these claims are readable upon the elected invention.

Should applicant traverse on the ground that the inventions are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Rejoinder

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

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During a telephone conversation with Sunhee Lee on February 17 2010 a provisional election was made without traverse to prosecute the invention of Group I, claims 1-15. Affirmation of this election must be made by applicant in replying to this Office action. Claims 16-17 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Claims **1-15** are examined on the merits herein.

Priority

Receipt is acknowledged of a certified copy of the priority document *in this National Stage application from the International Bureau* submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

The information disclosure statements (IDS) submitted on 10/6/06 and 12/6/06 were considered by the examiner.

Specification

The use of the trademark ZOCOR (pages 18-19) has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

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The disclosure is objected to because of the following informalities: xanthan gum is incorrectly spelt as xantan gum on at least pages 7-8.

Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

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consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3-7 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gutierrez-Rocca et al. (US Patent No. 6524615).

Applicant Claims

The instant application claims a sustained release formulation comprising a HMG-CoA reductase inhibitor, a solubilizing agent, a stabilizing agent, a carrier and a gel hydration accelerator.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Gutierrez-Rocca et al. claim a sustained or prolonged release pharmaceutical unit dosage form comprising a hard shell capsule and a formulation comprising (1) water insoluble medicament such as atorvastatin, simvastatin, lovastatin (all HMG-CoA reductase inhibitors); (2) a high melting fatty acid ester; (3) low viscosity oil (wherein 2 and 3 read on carrier); (4) a cellulosic polymer such as methocel E series and K series which read on gel hydration accelerator; (4) a non-ionic surfactant such as poloxamers and d-2-tocopheryl polyethylene glycol 1000 succinate (which read on solubilizer) (claim 1). It is taught that pharmaceutically acceptable excipients can be added such as stabilizers/antioxidants like butylated hydroxyl toluene or ascorbic acid (column 6, lines 6-8). It is taught that that the incorporation of lubricants like waxes and high melting glyceride in tablet matrices have been a popular method to prolong drug release (column 1, lines 64-65). Suitable carriers for the invention include high melting fatty

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acid ester esters, low viscosity oils and cellulosic polymers (column 3, lines 52-64). An exemplified formulation comprises lovastatin, compritol 888 and olive oil (3.8 weight part), methocel K100M (0.15 weight part), polysorbate 80 (0.05 weight part).

**Ascertainment of the Difference Between Scope the Prior Art and the Claims
(MPEP §2141.012)**

While Gutierrez-Rocca et al. teach that the composition can comprise excipients such as stabilizers/antioxidants like butylated hydroxyl toluene or ascorbic acid, Gutierrez-Rocca et al. do not exemplify formulations comprising these stabilizers.

While Gutierrez-Rocca et al. claim the statin can be simvastatin, Gutierrez-Rocca et al. do not exemplify formulations comprising simvastatin.

While Gutierrez-Rocca et al. claim the surfactant can be a poloxamer or d-2-tocopheryl polyethylene glycol 100 succinate, Gutierrez-Rocca et al. do not exemplify these surfactants.

**Finding of Prima Facie Obviousness Rationale and Motivation
(MPEP §2142-2143)**

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to utilize a stabilizer such as ascorbic acid or butylated hydroxyl toluene in the sustained release composition. One of ordinary skill in the art would have been motivated to utilize a stabilizer as they are excipients taught by Gutierrez-Rocca et al. that can be included. Therefore, one of ordinary skill in the art would have been motivated to add them in order to stabilize the sustained release formulations as taught by Gutierrez-Rocca et al.

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It would have been obvious to one of ordinary skill in the art at the time of the instant invention to utilize simvastatin as the medicament. One of ordinary skill in the art would have been motivated to utilize simvastatin as it is a specifically claimed medicament. One of ordinary skill in the art would have been motivated to replace the exemplified lovastatin with simvastatin as both are taught by Gutierrez-Rocca et al. as functional equivalents. Further more, the selection of a specific drug is considered *prima facie* obvious depending on the desired condition/symptoms to be treated.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to utilize a poloxamer or d-2-tocopheryl polyethylene glycol 100 succinate as the surfactant. One of ordinary skill in the art would have been motivated to utilize these surfactants as they are ones specifically claimed. One of ordinary skill in the art would have been motivated to replace the exemplified polysorbate 80 with a poloxamer or d-2-tocopheryl polyethylene glycol 100 succinate as all are taught by Gutierrez-Rocca et al. as functional equivalents.

Regarding claim 15, the high melting glycerides read on lubricant.

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the instantly claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claim 2 is rejected under 35 U.S.C. 103(a) as being unpatentable over Gutierrez-Rocca et al. in view of Serajuddin et al. (US Patent No. 5433951).

Applicant Claims

The instant application claims the solubilizing agent is 0.05 to 20 weight part; the stabilizing agent is 0.01 to 0.1 weight part; the sustained release composite carrier is 3 to 30 weight part; and the gel hydration accelerator is 0.1 to 5 weight part based on 1 weight part of the HMG- CoA reductase inhibitor.

**Determination of the Scope and Content of the Prior Art
(MPEP §2141.01)**

The teachings of Gutierrez-Rocca et al. are set forth above. Specifically, Gutierrez-Rocca et al. exemplify a formulation comprises lovastatin, compritol 888 and olive oil (3.8 weight part), methocel K100M (0.15 weight part), polysorbate 80 (0.05 weight part). Other non-ionic surfactant taught include poloxamers and d-2-tocopheryl polyethylene glycol 1000 succinate. It is taught that pharmaceutically acceptable excipients can be added such as stabilizers/antioxidants like butylated hydroxyl toluene or ascorbic acid (column 6, lines 6-8).

**Ascertainment of the Difference Between Scope the Prior Art and the Claims
(MPEP §2141.012)**

While Gutierrez-Rocca et al. teach stabilizers can be added, Gutierrez-Rocca et al. do not teach amounts that are suitable. However, this deficiency is cured by Serajuddin et al.

Serajuddin et al. is directed to sustained release formulations. It is taught that antioxidants for fatty acid glycerides such as ascorbic acid or butylated hydroxy toluene can be present in an amount within the range from about 0.005 to about 2%, preferably from about 0.01 to about 1% (column 3, lines 51-27).

***Finding of Prima Facie Obviousness Rationale and Motivation
(MPEP §2142-2143)***

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the teachings of Gutierrez-Rocca et al. and Serajuddin et al. and utilize the antioxidants in an amount from about 0.005 to about 2%. One of ordinary skill in the art would have been motivated to utilize this amount as the antioxidants are taught by Gutierrez-Rocca et al. as being suitable to add and the compositions comprise fatty acid glycerides and Serajuddin et al. teach this is an amount suitable to stabilize fatty acid glycerides. Therefore, one of ordinary skill in the art would have been motivated to utilize the antioxidants in this amount based on the teachings of Serajuddin et al.

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the instantly claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 8-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gutierrez-Rocca et al. in view of Baichwal et al. (US Patent No. 5135757) as evidenced by Mosquera et al. (Int. J. Pharmaceutics, 1996).

Applicant Claims

The instant application claims the composition comprises sodium alginate, xanthan gum, locust bean gum, propylene glycol ester alginate and hydroxypropyl methylcellulose.

**Determination of the Scope and Content of the Prior Art
(MPEP §2141.01)**

The teachings of Gutierrez-Rocca et al. are set forth above. Specifically, Gutierrez-Rocca et al. exemplify a formulation comprises lovastatin, compritol 888 and olive oil (3.8 weight part), methocel K100M (0.15 weight part), polysorbate 80 (0.05 weight part). Other non-ionic surfactant taught include poloxamers and d-2-tocopheryl polyethylene glycol 1000 succinate. It is taught that pharmaceutically acceptable excipients can be added such as stabilizers/antioxidants like butylated hydroxyl toluene or ascorbic acid (column 6, lines 6-8).

**Ascertainment of the Difference Between the Prior Art and the Claims
(MPEP §2141.012)**

While Gutierrez-Rocca et al. teach that the sustained release formulation comprises cellulosic polymers such as methocel K100M, Gutierrez-Rocca et al. do not teach the inclusion of the hydrophilic polymers such as sodium alginate, locust bean gum, xanthan gum and propylene glycol ester alginate. However these deficiencies are cured by Baichwal et al.

Baichwal et al. is directed to compressible sustained release solid dosage forms. The invention provides a slow release granulation for use as a directly compressible pharmaceutical excipient. It comprises a heteropolysaccharide or a gum having similar

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properties and a polysaccharide material capable of crosslinking. The ratio of heteropolysaccharide to the polysaccharide material being from about 1:1 to about 4:1 (column 4, lines 40-47). Heteropolysaccharides taught include xanthan gum (column 5-6, lines 55-68 and 1-4). Crosslinking polysaccharides taught is preferably locust bean gum due to its higher ratio of mannose to galactose (column 6, lines 5-19). It is taught that other hydrophilic material can be added such as alginates, hydroxypropylmethyl cellulose and the like (column 6, lines 20-28). It is taught that certain other polysaccharide gums including alginic acid derivatives are believed to act synergistically with xanthan gum to produce matrices having high gel strength. The combination of xanthan gum with locust bean with or without the other polysaccharides gums is especially preferred. Known combinations which are known to produce synergistic results include propylene glycol alginate and sodium carboxymethylcellulose (column 6, lines 49-68). Specific compositions taught are xanthan gum, locust bean gum, propylene glycol alginate (example 23 and 24), xanthan gum, locust bean gum and hydroxypropylmethyl cellulose (Examples 25 and 26) and xanthan gum, locust bean gum and sodium alginate (example 27). The ratios of xanthan gum to locust bean gum to other hydrophilic material is 1:1:2.

***Finding of Prima Facie Obviousness Rationale and Motivation
(MPEP §2142-2143)***

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the teachings of Gutierrez-Rocca et al. and Baichwal et al. and utilize a combination of heteropolysaccharides and polysaccharides in the sustained release composition of Gutierrez-Rocca et al. One of ordinary skill in the art

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would have been motivated to utilize a combination of heteropolysaccharides and polysaccharides as Baichwal et al. teach that combination act synergistically to provide matrices having high gel strength. Specific combinations taught include xanthan gum, locust bean gum, propylene glycol alginate; xanthan gum, locust bean gum and hydroxypropylmethyl cellulose; and xanthan gum, locust bean gum and sodium alginate. Therefore, it would have been obvious to one of ordinary skill in the art to manipulate the hydrophilic polymers utilized in order to obtain a synergistic combination for increasing gel strength as taught by Baichwal et al.

Regarding the claimed amount of the hydrophilic polymers is 1 part xanthan gum, 1 part locust bean gum and 2 parts of other hydrophilic material. These amounts read on the amounts claimed. The amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ and reasonably would expect success. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient to add in order to best achieve the desired results. It would have been obvious to one of ordinary skill in the art to manipulate the amount of polysaccharides in order to determine amounts which produce synergistic results as taught by Baichwal et al. It would have been obvious to one of ordinary skill in the art at the time of the invention to engage in routine experimentation to determine optimal or workable ranges that produce expected results. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or

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workable ranges by routine experimentation. *In re Aller*, 220 F. 2d 454, 105 USPQ 233 (CCPA 1955).

Regarding claim 14, as evidenced by Mosquera et al. Methocel K100M has a viscosity of 100,000 CP (page 147).

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the instantly claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 1, 3-4 and 7-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Louie-Helm et al. (USPGPUB No. 20030091630) in view of Baichwal et al.

Applicant Claims

The instant application claims a sustained release formulation comprising a HMG-CoA reductase inhibitor, a solubilizing agent, a stabilizing agent, a carrier and a gel hydration accelerator.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Louie-Helm et al. is directed to a formulation of an erodible gastric retentive oral dosage form. The invention provides a controlled release dosage form (paragraph 006). Sellable, bioerodible polymers which determine the rate at which the polymer matrix erodes include cellulosic polymers such as hydroxypropyl methylcellulose with

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viscosity in the range of about 50 to 110,000 (paragraph 0059, 0063 and 0082) and polysaccharide gums such as xanthan gum (paragraph 0079 and 0084) as well as natural polymers such as alginates (paragraph 0086).. It is taught that the water-swelling polymers can be used individually or in combination. Examples of combination include a cellulosic polymer combined with a gum such as hydroxypropylcellulose with xanthan gum (paragraph 0090). The amount of polymer relative to the drug can vary depending the polymer used, molecular weight and excipients that may be present (paragraph 0093). Ranges of drug to polymer claimed is from about 1:500 to about 85:15 (claim 13). Drugs taught include HMG-CoA reductase inhibitors such as simvastatin and lovastatin (paragraph 0110 and claim 23). Tablets prepared for oral administration will generally contain other materials such as binders, lubricants, stabilizers, surfactants (solubility enhancers). Stabilizers are used to inhibit or retard drug decomposition reactions (paragraph 0129).

**Ascertainment of the Difference Between Scope the Prior Art and the Claims
(MPEP §2141.012)**

While Louie-Helm et al. teach solubilizers and stabilizers can be added, Louie-Helm et al. do not exemplify formulations comprising these ingredients.

While, Louie-Helm et al. teach that the matrix can be made from cellulosic polymers, gums and alginates and combinations thereof, Louie-Helm et al. do not exemplify formulations comprising sodium alginate, xanthan gum and locust bean gum or hydroxypropyl methylcellulose, propylene glycol ester alginate and the other polymers. However, this deficiency is cured by Baichwal et al.

Baichwal et al. is directed to compressible sustained release solid dosage forms. The invention provides a slow release granulation for use as a directly compressible pharmaceutical excipient. It comprises a heteropolysaccharide or a gum having similar properties and a polysaccharide material capable of crosslinking. The ratio of heteropolysaccharide to the polysaccharide material being from about 1:1 to about 4:1 (column 4, lines 40-47). Heteropolysaccharides taught include xanthan gum (column 5-6, lines 55-68 and 1-4). Crosslinking polysaccharides taught is preferably locust bean gum due to its higher ratio of mannose to galactose (column 6, lines 5-19). It is taught that other hydrophilic material can be added such as alginates, hydroxypropymethyl cellulose and the like (column 6, lines 20-28). It is taught that certain other polysaccharide gums including alginic acid derivates are believed to act synergistically with xanthan gum to produce matrices having high gel strength. The combination of xanthan gum with locust bean with or without the other polysaccharides gums is especially preferred. Known combinations with are known to produce synergistic results include propylene glycol alginate and sodium carboxymethylcellulose (column 6, lines 49-68). Specific compositions taught are xanthan gum, locust bean gum, propylene glycol alginate (example 23 and 24), xanthan gum, locust bean gum and hydroxypropylmethyl cellulose (Examples 25 and 26) and xanthan gum, locust bean gum and sodium alginate (example 27). The ratios of xanthan gum to locust bean gum to other hydrophilic material is 1:1:2

***Finding of Prima Facie Obviousness Rationale and Motivation
(MPEP §2142-2143)***

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It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the teachings of Louie-Helm et al. and Baichwal et al. and utilize a combination of heteropolysaccharides and polysaccharides in the sustained release composition of Louie-Helm et al. One of ordinary skill in the art would have been motivated to utilize a combination of heteropolysaccharides and polysaccharides as Louie-Helm teach these polymers can be utilized and suggest combinations of polymers like xanthan gum and cellulosic polymers and Baichwal et al. teach that combinations act synergistically to provide matrices having high gel strength. Specific combinations taught include xanthan gum, locust bean gum, propylene glycol alginate; xanthan gum, locust bean gum and hydroxypropylmethyl cellulose; and xanthan gum, locust bean gum and sodium alginate. Therefore, it would have been obvious to one of ordinary skill in the art to manipulate the hydrophilic polymers utilized in order to obtain a synergistic combination for increasing gel strength as taught by Baichwal et al.

Regarding the claimed amount of the hydrophilic polymers is 1 part xanthan gum, 1 part locust bean gum and 2 parts of other hydrophilic material. These amounts read on the amounts claimed. The amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ and reasonably would expect success. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient to add in order to best achieve the desired results. It would have been obvious to one of ordinary skill in the art to manipulate the amount of

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polysaccharides in order to determine amounts which produce synergistic results as taught by Baichwal et al. It would have been obvious to one of ordinary skill in the art at the time of the invention to engage in routine experimentation to determine optimal or workable ranges that produce expected results. Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F. 2d 454, 105 USPQ 233 (CCPA 1955).

Regarding claim 14, the viscosity of the cellulosic polymers taught by Louie-helm et al. overlap those instantly claimed. In the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a *prima facie* case of obviousness exists.

See MPEP 2144.05 [R-5]

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the instantly claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 1 and 3-15 are provisionally rejected under 35 U.S.C. 103(a) as being obvious over copending Application No. 10650931 (Woo et al., PG PUB No. 20040081693) which has a common inventor with the instant application in view of Gutierrez-Rocca et al. Based upon the earlier effective U.S. filing date of the copending application, it would constitute prior art under 35 U.S.C. 102(e) if published or patented. This provisional rejection under 35 U.S.C. 103(a) is based

upon a presumption of future publication or patenting of the conflicting application.

This provisional rejection might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the copending application was derived from the inventor of this application and is thus not the invention “by another,” or by a showing of a date of invention for the instant application prior to the effective U.S. filing date of the copending application under 37 CFR 1.131. This rejection might also be overcome by showing that the copending application is disqualified under 35 U.S.C. 103(c) as prior art in a rejection under 35 U.S.C. 103(a). See MPEP § 706.02(I)(1) and § 706.02(I)(2).

Applicant Claims

The instant application claims a sustained release formulation comprising a HMG-CoA reductase inhibitor, a solubilizing agent, a stabilizing agent, a carrier and a gel hydration accelerator.

**Determination of the Scope and Content of the Prior Art
(MPEP §2141.01)**

Woo et al. claim a sustained release composition comprising a mixture of sodium alginate and xanthan gum, hydroxypropylmethylcellulose and propylene glycol alginate (claim 2). The ratio of drug: carrier:accelerator is 1:3-30:0.1-15 (claim 3). The weight ratio of sodium alginate and xanthan gum is 1:0.1-10 (claim 4). The composition further comprises locust bean gum (claim 5). Ratio of sodium alginate:xanthan gum:locust bean gum is 1:0.2-10:0.1-5 (claim 6). Weight ratio of hydroxy propylmethylcellulose and

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propylene glycol alginate is in the range of 1:0.05-20 (claim 7). Drugs include drugs for hyperlipidemia (claim 8) such as lovastatin (claim 9). Other drugs for hyperlipidemia taught include simvastatin (paragraph 0022). It is taught that the composition may additionally include stabilizers, lubricants, wetting agents, flavoring agent, emulsifiers and the like (paragraph 0030).

**Ascertainment of the Difference Between Scope the Prior Art and the Claims
(MPEP §2141.012)**

While Woo et al. teach that the composition can comprise simvastatin, stabilizers, emulsifiers and other excipients like flavoring agents, Woo et al. do not exemplify these combinations.

While Woo et al. teach stabilizers and emulsifiers can be added, Woo et al. do not specify specific examples of these components. However, this deficiency is cured by Gutierrez-Rocca et al.

Gutierrez-Rocca et al. claim a sustained or prolonged release pharmaceutical unit dosage form comprising a hard shell capsule and a formulation comprising (1) water insoluble medicament such as atorvastatin, simvastatin, lovastatin (all HMG-CoA reductase inhibitors); (2) a high melting fatty acid ester; (3) low viscosity oil (wherein 2 and 3 read on carrier); (4) a cellulosic polymer such as methocel E series and K series which read on gel hydration accelerator; (4) a non-ionic surfactant such as poloxamers and d-2-tocopheryl polyethylene glycol 1000 succinate (which read on solubilizer) (claim 1). It is taught that pharmaceutically acceptable excipients can be added such as stabilizers/antioxidants like butylated hydroxyl toluene or ascorbic acid (column 6, lines 6-8).

***Finding of Prima Facie Obviousness Rationale and Motivation
(MPEP §2142-2143)***

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the teachings of Woo et al. and Gutierrez-Rocca et al. and utilize stabilizer and solubilizer in the sustained release formulation of Woo et al. One of ordinary skill in the art would have been motivated to utilize these components as Woo et al. suggest that they can be utilized in the formulations. Therefore, it would have been obvious to one of ordinary skill to add these components in order to aid in solubilization and stabilization as taught by Woo et al.

Regarding the specifically, claimed stabilizers and solubilizers, Gutierrez-Rocca et al. teach stabilizers/antioxidants like butylated hydroxyl toluene or ascorbic acid and surfactant such as poloxamers and d-2-tocopheryl polyethylene glycol 1000 succinate which are taught as being suitable for use with statins. Therefore, it would have been obvious to choose these specific stabilizers and surfactants as they are known to be utilized in sustained release formulations wherein the active agent is a statin.

Absent any evidence to the contrary, and based upon the teachings of the prior art, there would have been a reasonable expectation of success in practicing the instantly claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-15 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 5-6, 8 and 10 of copending Application No. 10650931 in view of Gutierrez-Rocca et al. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims overlap in scope.

The instant application claims a sustained release formulation comprising a HMG-CoA reductase inhibitor, a solubilizing agent, a stabilizing agent, a carrier and a gel hydration accelerator.

Copending '931 claims a sustained release formulation comprising lovastatin (drugs also claimed include drugs for hyperlipidemia), a carrier and a gel hydration

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accelerator. The sustained release composition comprising a mixture of sodium alginate and xanthan gum, hydroxypropylmethylcellulose and propylene glycol alginate. The ratio of drug: carrier:accelerator is 1:3-30:0.1-15. The weight ratio of sodium alginate and xanthan gum is 1:0.1-10. The composition further comprises locust bean gum. Ratio of sodium alginate:xanthan gum:locust bean gum is 1:0.2-10:0.1-5. Weight ratio of hydroxy propylmethylcellulose and propylene glycol alginate is in the range of 1:0.05-20.

Copending '931 does not claim the composition comprise a stabilizer or a solubilizer. However, this deficiency is cured by Gutierrez-Rocca et al.

Gutierrez-Rocca et al. claim a sustained or prolonged release pharmaceutical unit dosage form comprising a hard shell capsule and a formulation comprising (1) water insoluble medicament such as atorvastatin, simvastatin, lovastatin (all HMG-CoA reductase inhibitors); (2) a high melting fatty acid ester; (3) low viscosity oil (wherein 2 and 3 read on carrier); (4) a cellulosic polymer such as methocel E series and K series which read on gel hydration accelerator; (4) a non-ionic surfactant such as poloxamers and d-2-tocopheryl polyethylene glycol 1000 succinate (which read on solubilizer) (claim 1). It is taught that pharmaceutically acceptable excipients can be added such as stabilizers/antioxidants like butylated hydroxyl toluene or ascorbic acid (column 6, lines 6-8). It is taught that that the incorporation of lubricants like waxes and high melting glyceride in tablet matrices have been a popular method to prolong drug release (column 1, lines 64-65). Suitable carriers for the invention include high melting fatty acid ester esters, low viscosity oils and cellulosic polymers (column 3, lines 52-64). An

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exemplified formulation comprises lovastatin, compritol 888 and olive oil (3.8 weight part), methocel K100M (0.15 weight part), polysorbate 80 (0.05 weight part).

It would have been obvious to one of ordinary skill in the art to combine the teachings of Copending ' 931 and Gutierrez-Rocca et al. and add a stabilizer and solubilizer to the composition of copending '931. One of ordinary skill in the art would have been motivated to add these components as they are taught as pharmaceutically acceptable excipients. It would have been obvious to one of ordinary skill in the art to add customary excipients which are utilized to enhance formulations comprising statins. Therefore, one of ordinary skill in the art would have been motivated to add these components to aid in solubilization and stability of the compositions as taught by Gutierrez-Rocca et al.

Therefore, the scopes of the copending claims and the instant application overlap and thus they are obvious variants of one another.

This is a provisional obviousness-type double patenting rejection.

It is noted that in application 10650931 a notice of allowance has been mailed. . However, the rejection will remain provisional until the time that a patent number is associated with application 10650931.

Conclusion

No claims are allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to ABIGAIL FISHER whose telephone number is (571)270-3502. The examiner can normally be reached on M-Th 9am-6pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Abigail Fisher
Examiner
Art Unit 1616

AF

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Primary Examiner, Art Unit 1616